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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/491,974	01/27/00	SCHMALJOHN C	003/115/SAP

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1632	11

DATE MAILED: 08/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/491,974	SCHMALJOHN ET AL.	
	Examin r	Art Unit	
	Peter Brunovskis	1632	

-- The MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,7,9,10,12,13,16-20,22-24,26 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7,9,10,12,13,16-20,22-24,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The response filed 6/04/01 (Paper No. 9) has been entered. Amendment of claims 1, 7, 9, 10, 16, 17, 26, and 27 and cancellation of claims 2, 5, 6, 8, 11, 14, 15, 21, and 25 is acknowledged.

Any objections or rejections made in a previous Office Action that are not herein reinstated have been withdrawn. Unless otherwise indicated, arguments directed to rejections rendered moot by Applicants amendments or Examiner's withdrawal will not be further addressed or acknowledged. Claims 1, 3, 4, 7, 9, 10, 12, 13, 16-20, 22-24, 26, and 27 are pending in the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 10, 12, 13, 16-20, 22-24, 26, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9, step (i) (and dependent claims) is indefinite in its recitation of the phrase "operatively linked to a promoter" since it is unclear whether this phrase is directed to the antigenic determinant or the nucleic acid encoding the M gene segment protein. Amending step (i) to recite --preparing a nucleic acid encoding a hantavirus M gene segment protein comprising the sequence set forth in SEQ ID NO:1 operatively linked to a promoter active in cells of a mammal, wherein said M gene segment protein includes at least one antigenic determinant-- would obviate the rejection.

Claim 9 (and dependent claims) is indefinite because it is not clear how detection step (iv) relates back to the preamble which recites a method for inducing a protective immune response to a hantavirus protein". Deleting "and" in step (iii) and substituting step (iv) with the phrase --to generate an immune response sufficient for protection against a hantaviral challenge in said mammal-- would obviate the rejection.

Claim 16 is indefinite because it is unclear what the phrase "the sequence" (singular) is directed to: SEQ ID NO:1 only or SEQ ID NO:1 and SEQ ID NO:2. If the latter, Applicants should amend the claim to recite the phrase "the sequences set forth in..." Further, it is unclear how the nucleic acid of claim 16, comprising two distinct genes relates back to the subject matter in step (i) of base claim 9 (or further limits) drawn to a method comprising a nucleic acid operatively linked to a promoter linked to an M gene segment.

Claim 17 is indefinite because it is not clear how detection step (iv) relates back to the preamble which recites a method for inducing a protective immune response to a hantavirus

infection". Further it is not clear how the claimed subject matter in this claim differs in scope with that of claim 9. Deleting "and" in step (iii) and substituting step (iv) with the phrase --to generate an immune response sufficient for protection in said mammal to a hantaviral challenge comprising a viral isolate distinct from one carrying the sequence set forth in SEQ ID NO:1-- would obviate the rejection.

Claim 24 is indefinite because it depends on a cancelled claim.

Claim 26 (and dependent claims) is indefinite in its recitation of the term "first hantavirus" since no "second hantavirus" is recited in the claim.

Claims 26 and 27 are indefinite in their recitation of the phrases "one or more DNA sequences coated onto the..." since *sequences* lack any form or structure. Moreover, coating of DNA sequences onto a promoter makes even less sense. Amending the claims to better reflect the nature of the *nucleic acids* comprising said sequences and the appropriate substances coated (i.e. carrier particles as opposed to promoters) would obviate the basis for this rejection.

Claims 26 is indefinite because it is unclear what structural relationship exists between the one or more DNA sequences, the sequence of SEQ ID NO:1, the operatively linked promoters, the carrier particles, the antigenic determinants (or sequences thereof), and the nucleic acids which are implicit in the claimed composition..

Claim 27 is indefinite because it is unclear what structural relationship exists between claim 27 and base claim 26. Specifically, it is unclear what structural relationship exists between the one or more DNA sequences, the "first hantavirus", the "second hantavirus", the sequence of

SEQ ID NO:1, the operatively linked promoters, the carrier particles, the antigenic determinants (or sequences thereof), and the nucleic acids which are implicit in the claimed composition. For example, it is unclear whether the claim is drawn to multiple different and distinct nucleic acids each containing different hantaviral sequences comprising SEQ ID NO:1, wherein each is operatively linked to a promoter with or without additional associated antigenic determinants wherein each nucleic acid is coated onto the carrier particle, or whether the claim is drawn to a single type of nucleic acid coated to the carrier particle which comprises one or more different hantaviral sequences, each operatively linked to an independent promoter.

Claim 27 is also indefinite because the claim recites DNA sequences comprising the sequence set forth in the SEQ ID NO:1, described in claim 26 as including an antigenic determinant *common* to any of the hantaviral members of the recited Markush on the one hand, but then further defines embodiments of claim 27 comprising the sequence set forth in the SEQ ID NO:1, wherein the sequence includes at least one or more *different* hantaviral antigenic determinants. It is not clear whether the claims include antigenic determinant sequences additional and distinct from any directed to the sequence of SEQ ID NO:1. Further, inasmuch as the nature of the antigenic determinants are unclear with respect to their structural relationship to protein encoded by SEQ ID NO:1, it is not clear whether the subject matter of claim 27 (or 26 for that matter) is structurally distinct from the composition of claim 1.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 12, 22, 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office Action of 3/01/01 and for the reasons set forth below as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 3, 12, 22, 26, and 27 are drawn to compositions or methods comprising an M gene segment comprising the sequence of SEQ ID NO:1 which encodes a protein that includes an antigenic determinant of a hantavirus protein, including one from Puumula virus. However, Example 6 of the instant specification teaches that plasmid pWRG-SEO-M which comprises the sequence of SEQ ID NO:1 fails to cross-protect against infection with Puumala virus. Thus, the prima facie evidence of record fails to provide support for SEQ ID NO:1 containing an antigenic determinant, particularly one associated with induction of protective immunity.

Claims 26 and 27 are drawn to vaccine compositions comprising a coding region for one or more antigenic determinant(s) of a hantavirus protein. The working examples clearly provide support for there being *an* antigenic determinant represented in the sequence of SEQ ID NO:1, at least with respect to Seoul virus, Hantaan virus, and Dobrava virus. However, claims 26 and 27 additionally recite antigenic determinant sequence limitations from which it cannot be clearly determined whether embodiments are embraced that comprise additional and distinct sequences

not present in SEQ ID NO:1 or patentably distinct from e.g. the composition of claim 1. Without clarification with respect to indefiniteness and/or an adequate written description concerning the specific nature of the antigenic determinants defining the nature of the similarities or differences between the various hantaviral isolates, one cannot clearly ascertain whether the rejected claims meet the written description requirement or whether a given embodiment necessarily anticipates the claimed subject matter of the rejected claims.

Applicant's arguments filed 6/04/01 have been fully considered but they are not persuasive. The response contends that the claims have been amended to specify that the protein coding region encodes an M gene segment protein comprising the sequence set forth in SEQ ID NO:1, which is asserted to contain at least one antigenic determinant of a hantavirus protein. However, this argument fails to address the problems as they relate to the newly amended subject matter, comprising new limitations directed to inoperative embodiments (e.g.. "wherein said hantavirus is Pumuula virus") or to embodiments comprising both common and different antigenic determinants, the nature of which have not been disclosed.

Claims 3, 9, 10, 12, 17, 22, 26, and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions or methods in mammals comprising M gene segments of the SEOV hantavirus comprising antigenic determinants for Seoul virus, Hantaan virus, and Dobrava virus, does not reasonably provide enablement for methods or compositions for inducing protection against hantaviruses, apart from Seoul virus,

Hantaan virus or Dobrava virus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As noted above, the newly amended claims are limited to methods or compositions comprising M gene segments comprising SEQ ID NO:1 from the SEOV hantavirus. However, the reject claims embrace limitations directed to antigenic determinants that are not necessarily present in the full range of hantaviruses as listed in the instant claims. Given that Example 6 of the instant specification teaches that plasmid pWRG-SEO-M fails to cross-protect against infection with Puumala virus and comprises the sequence of SEQ ID NO:1, Applicants are not enabled for the full scope of the claimed subject matter directed to other hantaviral isolates. Since the prima facie evidence of record fails to provide support for SEQ ID NO:1 containing an antigenic determinant for any and all hantaviruses, the invention is not enabled for the full scope with the subject matter as claimed.

Applicant's arguments filed 6/04/01 have been fully considered but they are not persuasive. The response contends that cross-protection is dictated by the extent of genetic relatedness, which accounts for the cross-protection between Hantaan, Seoul and Dobrava having >80% amino acid identity, contrasted with only 52% amino acid homology with Puumala virus, for which cross-protection was not observed. In view of the unpredictability associated with protective immunity as set forth in the Office Action of 3/01/01, absent experimental evidence to the contrary, the compositions or methods can only be enabled for those compositions comprising established

antigenic determinants to defined hantaviral species or for those methods directed to use of SEQ ID NO:1-containing compositions experimentally determined to protect against the particular hantaviral species that are in accordance with the claimed methods. Inasmuch as polynucleotides comprising SEQ ID NO:1 have been shown to protect against multiple different hantaviruses and it would not require undue experimentation to determine operative from inoperative embodiments, Applicants *would* be enabled for methods of inducing protective immunity against hantaviruses, recited in a generic context.

Claims 1, 4, and 7 are allowed.

The claimed subject matter appears to be free of the art and would be allowable upon amending the claims so they are clearly limited to embodiments comprising SEQ ID NO:1, wherein the antigenic determinants encoded therein are limited to sequences present in SEQ ID NO:1, wherein the compositions only recite hantaviral species commensurate with the antigenic determinant limitation in accordance with the empiric evidence, and wherein the methods are limited to cross-protection against particular hantaviral isolates empirically determined or directed to *generic* methods of protection against hantaviruses comprising nucleic acids containing SEQ ID NO:1.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX number is (703) 308-4242 or 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Brunovskis whose telephone number is (703) 305-2471. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda can be reached at (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Patent Analyst, Patsy Zimmerman whose telephone number is (703) 308-8338.

Peter Brunovskis, Ph.D.
Patent Examiner
Art Unit 1632

Deborah Crouch

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